

CLAIMS:

1. A method for detecting or determining delivery and expression of nucleic acid introduced into a cell comprising;
 - introducing labelled nucleic acid molecules that encode a reporter gene into cells;
 - detecting labelled cells as an indication of delivery of the nucleic acid into a cell; and
 - measuring the product of the reporter gene as an indication of DNA expression in the cell, whereby delivery and expression of nucleic acid molecules in the cell is detected or determined.
 2. The method of claim 1, wherein the labelled cells are detected by flow cytometry, fluorimetry, cell imaging or fluorescence spectroscopy.
 3. The method of claim 1, wherein the labelled cells are detected by flow cytometry
 4. The method of claim 1, wherein the nucleic acid molecule is DNA.
 5. The method of claim 1, wherein the label is iododeoxyuridine (IdU or IdUrd) or bromodeoxyuridine (BrdU).
 6. The method of claim 1, wherein the reporter gene encodes a fluorescent protein, or enzyme or antibody.
 7. The method of claim 6, wherein the enzyme is a luciferase, β -galactosidase or alkaline phosphatase.
 8. The method of claim 6, wherein the fluorescent protein is a red, green or blue fluorescent protein.
 9. The method of claim 16, step (a) comprises contacting the nucleic acid molecule is with a delivery agent that comprises a cationic compound.
 10. The method of claim 9, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoylphosphatidylethanolamine (DOPE),

2,3-dioleoyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propan-aminiumtrifluoroacetate (DOSPA), dioleoyl phosphatidylethanolamine (DOPE), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2 \cdot 4CF_3CO_2H$, $C_{40}H_{84}NO_3P \cdot CF_3CO_2H$, $C_{50}H_{103}N_7O_3 \cdot 4CF_3CO_2H$, $C_{55}H_{116}N_8O_2 \cdot 6CF_3CO_2H$,
 5 $C_{49}H_{102}N_6O_3 \cdot 4CF_3CO_2H$, $C_{44}H_{89}N_5O_3 \cdot 2CF_3CO_2H$, $C_{41}H_{78}NO_8P$, $C_{100}H_{206}N_{12}O_4S_2 \cdot 8CF_3CO_2H$, $C_{162}H_{330}N_{22}O_9 \cdot 13CF_3CO_2H$, $C_{43}H_{88}N_4O_2 \cdot 2CF_3CO_2H$, $C_{43}H_{88}N_4O_3 \cdot 2CF_3CO_2H$ and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride.

11. The method of claim 10, wherein the nucleic acid molecules
 10 are natural chromosomes, artificial chromosomes, fragments of a chromosome or naked DNA that is greater than at least about 0.6 megabase in size.

12. The method of claim 1, wherein the nucleic acid molecules are artificial chromosomes, plasmids, chromosome fragments, naked
 15 DNA, or natural chromosomes.

13. The method of claim 1, wherein the nucleic acid molecules are artificial chromosome expression systems (Aces).

14. The method of claim 1, wherein the cells are eukaryotic cells.

20 15. The method of claim 14, wherein the cells are primary cells, cell lines, plant cells, animal cells.

16. The method of claim 15, wherein the cells, are stem cells, nuclear transfer donor cells, tumor cells or transformed cells.

25 17. A method for monitoring the delivery of a nucleic acid molecule into a cell comprising:

- (a) labeling the nucleic acid molecule;
- (b) delivering labeled nucleic acid molecule into a cell; and
- (c) detecting labeled nucleic acid molecule in the cells by flow cytometry, fluorimetry, cell imaging or fluorescence spectroscopy, as an
 30 indication of delivery of nucleic acid molecule into the cells.

18. The method of claim 17, wherein the nucleic acid molecule is labeled with a thymidine analog.

19. The method of claim 18, wherein the thymidine analog is iododeoxyuridine or bromodeoxyuridine.

5 20. The method of claim 19, wherein a delivery agent comprises a cationic compound, and the nucleic acid molecule is treated therewith.

21. The method of claim 20, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoylphosphatidylethanolamine (DOPE),
 10 2,3-dioleoyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), dioleoyl phosphatidylethanolamine (DOPE), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2 \cdot 4CF_3CO_2H$, $C_{40}H_{84}NO_3P \cdot CF_3CO_2H$, $C_{50}H_{103}N_7O_3 \cdot 4CF_3CO_2H$, $C_{55}H_{116}N_8O_2 \cdot 6CF_3CO_2H$, $C_{49}H_{102}N_6O_3 \cdot 4CF_3CO_2H$, $C_{44}H_{89}N_5O_3 \cdot 2CF_3CO_2H$, $C_{41}H_{78}NO_8P$,
 15 $C_{100}H_{206}N_{12}O_4S_2 \cdot 8CF_3CO_2H$, $C_{162}H_{330}N_{22}O_9 \cdot 13CF_3CO_2H$, $C_{43}H_{88}N_4O_2 \cdot 2CF_3CO_2H$, $C_{43}H_{88}N_4O_3 \cdot 2CF_3CO_2H$ and (1-methyl-4-(1-octadec-9-enyl-nonadec-10-enylenyl) pyridinium chloride).

22. The method of claim 18, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a
 20 chromosome or naked DNA that is greater than at least about 0.6 megabase in size.

23. A method for screening agents for the ability to deliver nucleic acid molecule into a cell comprising:

(a) delivering a labeled nucleic acid molecule into the cell in the
 25 presence of the agent; and

(b) determine the number of cells containing the label, as an indication of the ability of the agent to deliver nucleic acid molecule into the cell.

24. The method of claim 23, wherein the number of cells is
 30 determined by flow cytometry, fluorimetry, cell imaging or fluorescence spectroscopy.

25. The method of claim 23, wherein the label is iododeoxyuridine or bromodeoxyuridine.

26. The method of claim 23, wherein the agent comprises a cationic compound.

- 5 27. The method of claim 26, wherein the compound is selected from the group consisting of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA), dioleoylphosphatidylethanolamine (DOPE), 2,3-dioleyloxy-N-[2(spermine-carboxamido)ethyl]-N,N-dimethyl-1-propanaminiumtrifluoroacetate (DOSPA), dioleoyl phosphatidylethanolamine
- 10 (DOPE), $C_{52}H_{106}N_6O_4 \cdot 4CF_3CO_2H$, $C_{88}H_{178}N_8O_4S_2 \cdot 4CF_3CO_2H$, $C_{40}H_{84}NO_3P \cdot CF_3CO_2H$, $C_{50}H_{103}N_7O_3 \cdot 4CF_3CO_2H$, $C_{55}H_{116}N_8O_2 \cdot 6CF_3CO_2H$, $C_{49}H_{102}N_6O_3 \cdot 4CF_3CO_2H$, $C_{44}H_{89}N_5O_3 \cdot 2CF_3CO_2H$, $C_{41}H_{78}NO_8P$, $C_{100}H_{206}N_{12}O_4S_2 \cdot 8CF_3CO_2H$, $C_{162}H_{330}N_{22}O_9 \cdot 13CF_3CO_2H$, $C_{43}H_{88}N_4O_2 \cdot 2CF_3CO_2H$, $C_{43}H_{88}N_4O_3 \cdot 2CF_3CO_2H$ and (1-methyl-4-(1-octadec-
- 15 9-enyl-nonadec-10-enylenyl) pyridinium chloride.

28. The method of claim 23, wherein the nucleic acid molecule is a natural chromosome, an artificial chromosome, a fragment of a chromosome or naked DNA, or a plasmid

29. The method of claim 23, wherein the nucleic acid molecule is
- 20 a natural chromosome, an artificial chromosome, a fragment of a chromosome or naked DNA that is greater than at least about 0.6 megabase in size.

30. The method of claim 1, wherein the cell is selected from the group consisting of a primary cell, an immortalized cell, an embryonic
- 25 cell, a stem cell, a transformed cells and a tumor cell.

31. The method of claim 17, wherein the cell is selected from the group consisting of a primary cell, an immortalized cell, an embryonic cell, a stem cell, a transformed cells and a tumor cell.

32. The method of claim 23, wherein the cell is selected from
- 30 the group consisting of a primary cell, an immortalized cell, an embryonic cell, a stem cell, a transformed cells and a tumor cell.